ISSN 1070-4280, Russian Journal of Organic Chemistry, 2014, Vol. 50, No. 4, pp. 559–566. © Pleiades Publishing, Ltd., 2014.
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Bis[(tetraphenylporphyrinato)zinc]–Calix[4]pyrrole. Synthesis and Receptor Properties

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Received February 3, 2014

Abstract—A new bis[(tetraphenylporphyrinato)zinc]–calix[4]pyrrole conjugate has been synthesized from monoacetyl-substituted tetraphenylporphyrin, and its complexing ability toward 1,4-diazabicyclo[2.2.2]octane has been evaluated by spectrophotometric titration and ^{1}H NMR spectroscopy.

DOI: 10.1134/S1070428014040204

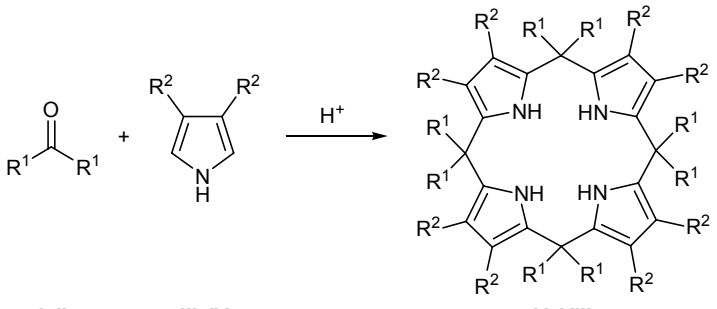
Calix[*n*]pyrroles constitute a specific class of conformationally mobile nonaromatic tetrapyrrole macrocycles which exhibit a strong complexing power toward ions and neutral molecules. Facile functionalization of these macrocyclic compounds makes it possible to use them as a molecular scaffold for building up preorganized three-dimensional receptors for definite substrates [1–10].

Relatively simple calix[4]pyrroles **V**–**VIII** symmetrically substituted at the *meso* and/or β-positions were synthesized (Scheme 1) by acid-catalyzed condensation of symmetric dialkyl ketones **I** and **II** with pyrroles **III** and **IV** having no substituents in positions *2* and *5* [2–6, 11–13]. Reactions of acetophenones with pyrrole gave calix[4]pyrroles **IX** and **X**, containing a methyl group and an aromatic substituents in each *meso* position [14]. Compounds **IX** and **X** are formed as mixtures of stereoisomers (αααα, αααβ, ααββ, αβαβ) differing by mutual arrangement of the alkyl and aryl substituents (Scheme 2); the αααα isomer has a *cone* conformation, while the other less symmetric isomers adopt *1,3-alternate* or *partial cone* structure.

Template condensation of tetraacetonylcalix[4]arene **XI** with pyrrole (Scheme 3) gave rise to covalently linked calix[4]pyrrole–calix[4]arene conjugate **XII** [15]. The authors noted formation of hydrogen bonds between the NH hydrogen atoms of the calix[4]pyrrole fragment and low-rim oxygen atoms of the calix[4]arene fragment.

Calix[4]pyrroles with two different substituents in the opposite *meso* positions are generally synthesized from dipyrromethanes. Calix[4]pyrroles **XV** and **XVI**

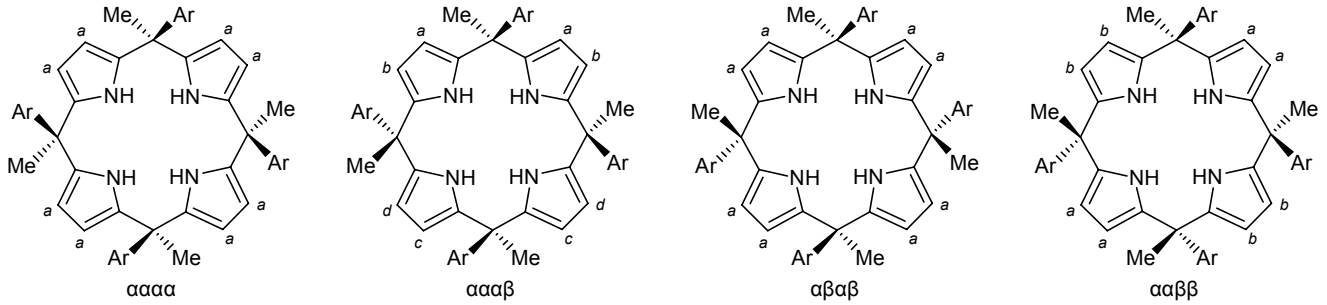
Scheme 1.



I, **II** **III**, **IV** **V**–**VIII**

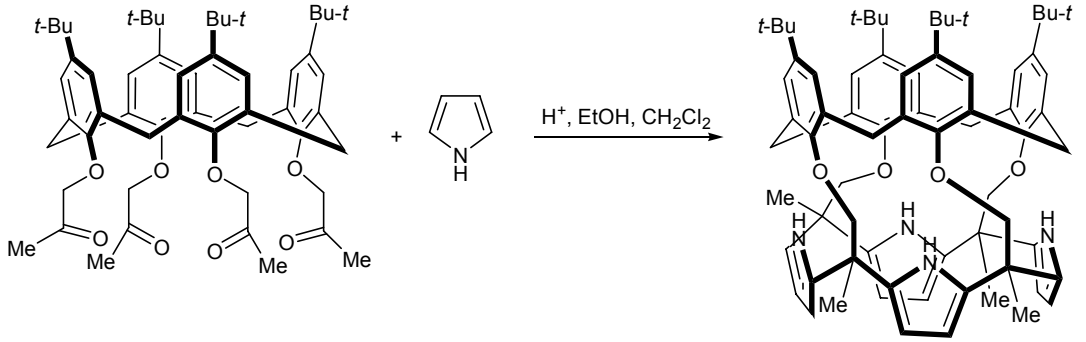
I, **V**, **VII**, R^1 = Me; **II**, **VI**, **VIII**, R^1 = Et; **III**, **V**, **VI**, R^2 = H; **IV**, **VII**, **VIII**, R^2 = F.

Scheme 2.



IX, Ar = HOC_6H_4; **X**, Ar = $MeOC_6H_4$.

Scheme 3.



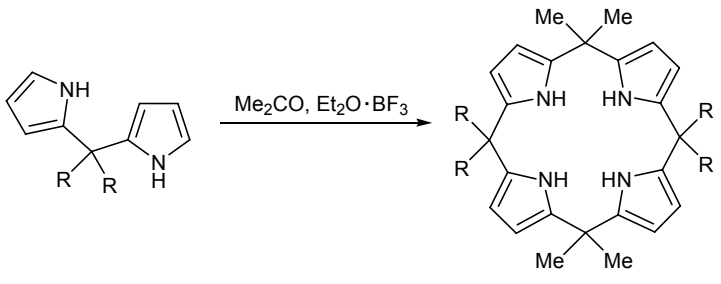
XI **XII**

were synthesized by reaction of *meso*-diaryl-substituted dipyrromethanes **XIII** and **XIV** with acetone in the presence of boron trifluoride–diethyl ether complex [16] (Scheme 4). The condensation of porphyrin–bis(dipyrromethane) **XVII** with acetone catalyzed by boron trifluoride–diethyl ether complex under high dilution conditions afforded calix[4]pyrrole-capped porphyrin as a mixture of conformational isomers **XVIII** and **XIX** with different orientations of the *meso*-methyl groups with respect to the porphyrin ring plane [17, 18] (Scheme 5). We previously synthesized bis(porphyrine)–calix[4]pyrrole **XXII** and its zinc complex **XXIII** by the Sonogashira reaction of bis(4-iodophenyl)calix[4]pyrrole **XX** with (5-ethynyloctaethylporphyrinato)zinc **XXI** [19, 20] (Scheme 6).

In the present article we describe the synthesis of new macrocyclic conjugates in which the calix[4]pyrrole scaffold holds two tetraphenylporphyrin fragments in a face-to-face orientation. The electronic absorption and ^{1}H NMR spectra of the synthesized compounds were consistent with the assigned structures, and they indicated strong mutual effect of π-electron systems of the porphyrin macrocycles.

Three-component condensation of pyrrole with benzaldehyde (**XXIV**) and 4-acetylbenzaldehyde (**XXV**) in acid medium on exposure to atmospheric

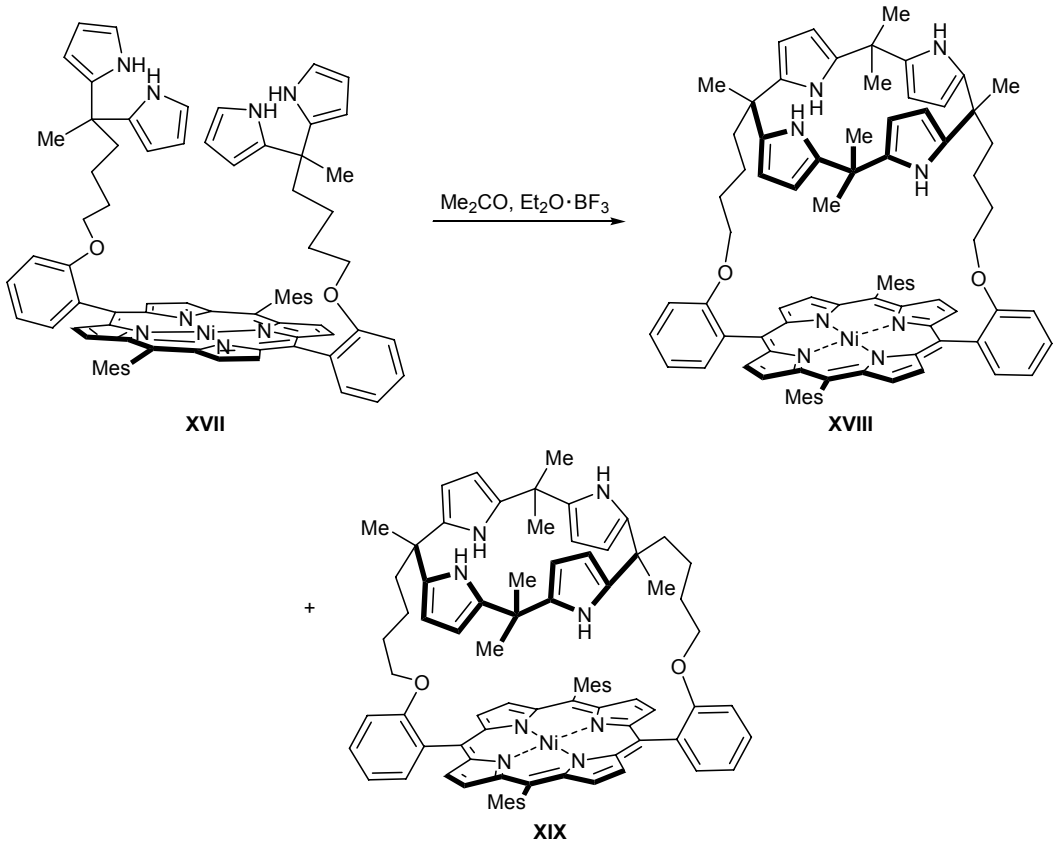
Scheme 4.



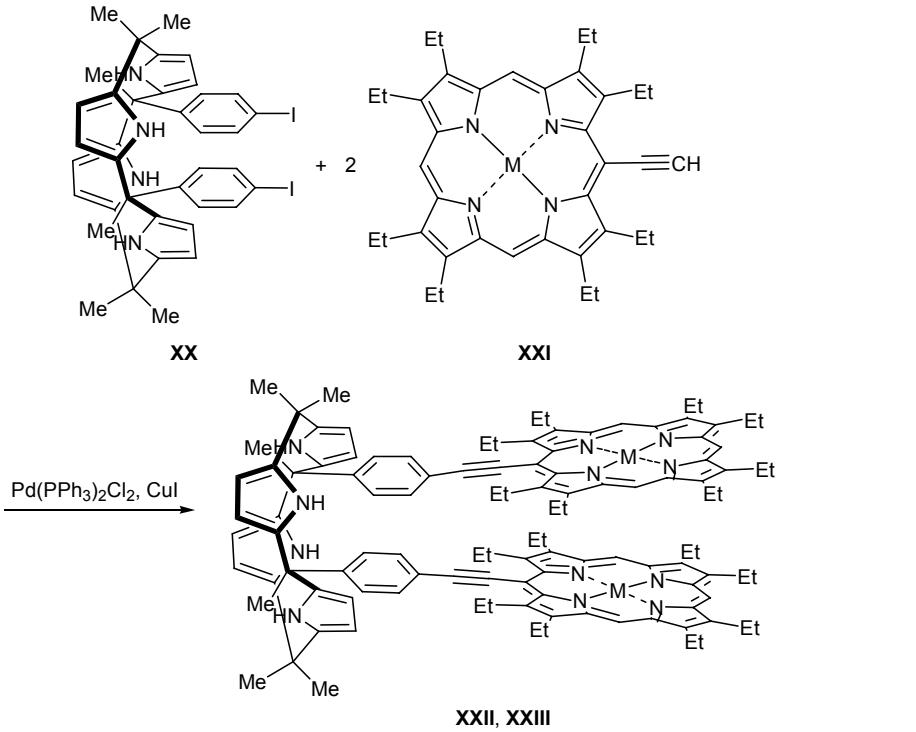
XIII, **XIV** **XV–XVI**

XIII, **XV**, R = Ph; **XIV**, **XVI**, R = pyridin-2-yl.

Scheme 5.

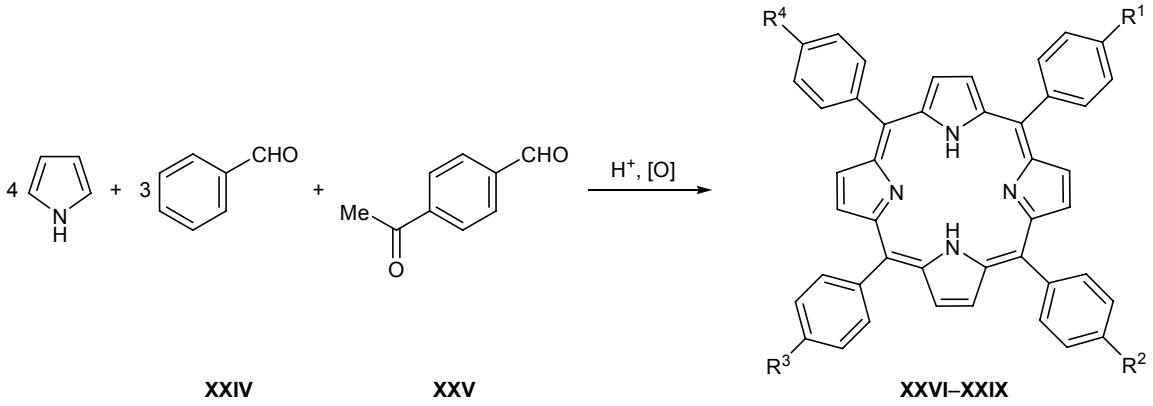


Scheme 6.



XXII, M = 2H; **XXIII**, M = Zn.

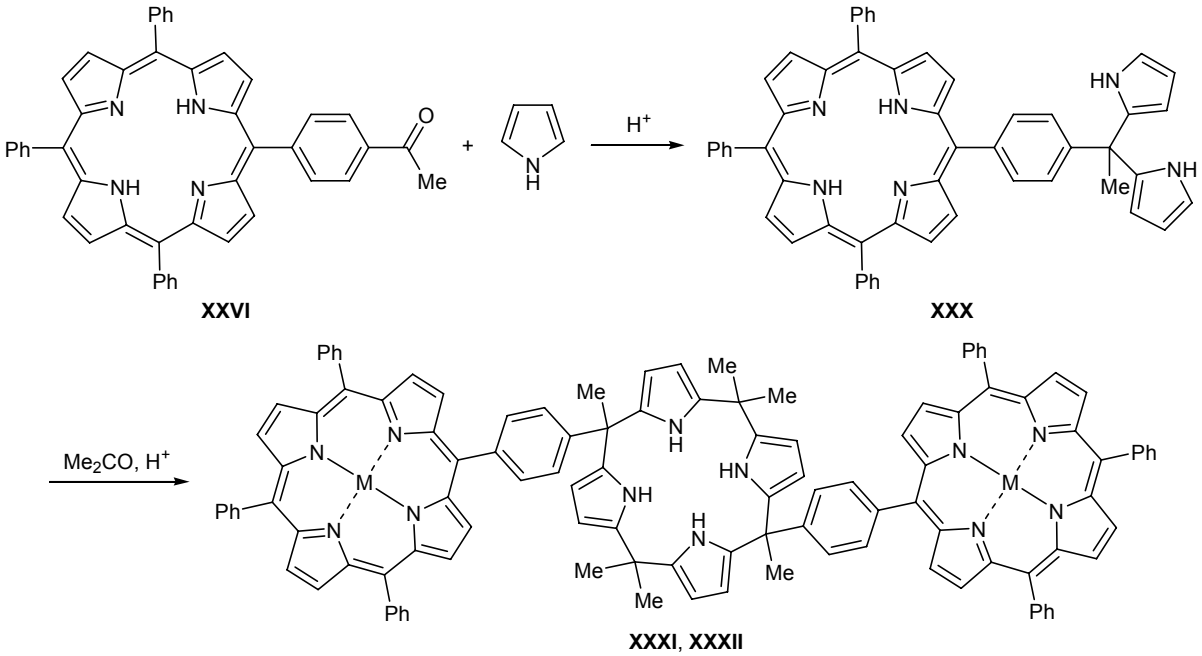
Scheme 7.



XXIV **XXV** **XXVI–XXIX**

XXVI, R^1 = MeCO, $R^2 = R^3 = R^4$ = H; **XXVII**, $R^1 = R^3$ = MeCO, $R^2 = R^4$ = H; **XXVIII**, $R^1 = R^2 = R^3 = R^4$ = MeCO; **XXIX**, $R^1 = R^2 = R^3 = R^4$ = H.

Scheme 8.



XXVI **XXX** **XXXI**, **XXXII**

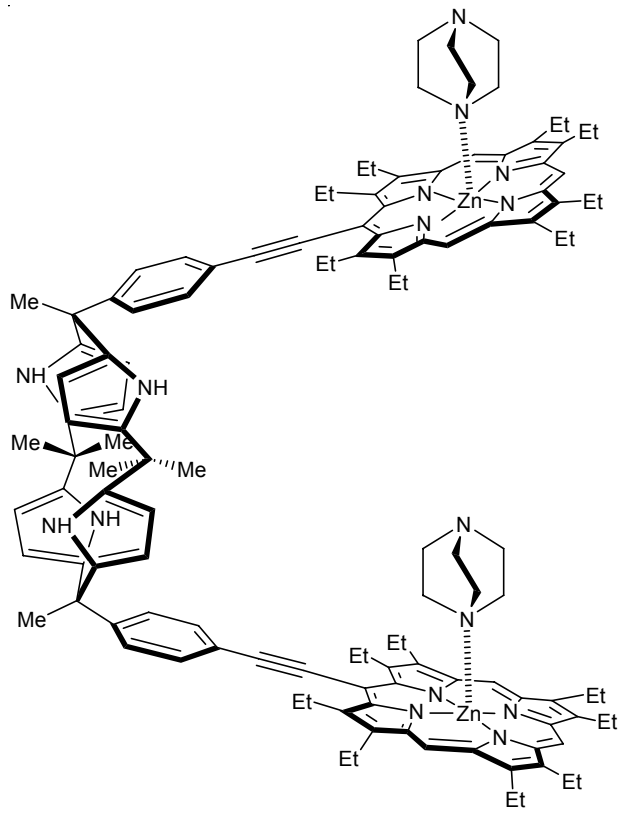
XXXI, M = 2H; **XXXII**, M = Zn.

moisture gave 5-(4-acetylphenyl)-10,15,20-triphenylporphyrin (**XXVI**) in 9% yield (Scheme 7). Apart from target product **XXVI**, we isolated from the reaction mixture small amounts of 5,15-bis(4-acetylphenyl)-10,20-diphenylporphyrin (**XXVII**), 5,10,15,20-tetrakis(4-acetylphenyl)porphyrin (**XXVIII**), and 5,10,15,20-tetraphenylporphyrin (**XXIX**).

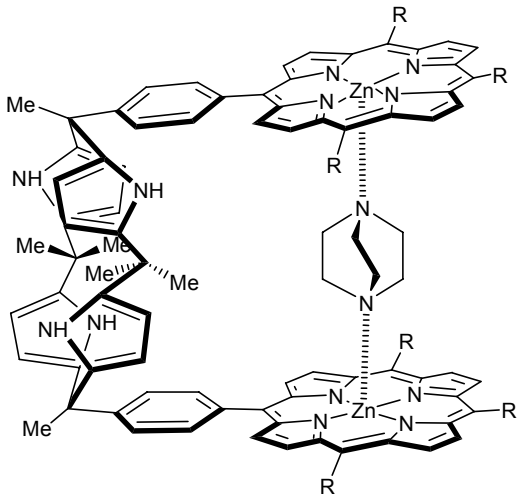
By reaction of acetyltetraphenylporphyrin **XXVI** with excess pyrrole under acidic conditions we obtained 5-[4-(5-methyldipyrromethan-5-yl)phenyl]-10,15,20-triphenylporphyrin (**XXX**) (Scheme 8) which reacted with excess acetone in acid medium to produce bis(porphyrin)–calix[4]pyrrole **XXXI** in 48% yield. The complexation of **XXXI** with zinc acetate in DMF afforded 90% of dinuclear zinc complex **XXXII**.

The ^{1}H NMR spectra of **XXXI** and **XXXII** contained signals belonging to protons in the calix[4]pyrrole and porphyrin fragments. The interaction between the π-electron systems of the porphyrin fragments in molecules **XXXI** and **XXXII** is clearly reflected in the upfield shifts of the NH and β-pyrrole proton signals relative to the corresponding signals of porphyrins **XXVI** and **XXX**. The signals from the β-pyrrole protons in the spectra of **XXXI** and **XXXII** are split,

Scheme 9.



XXIII–2L



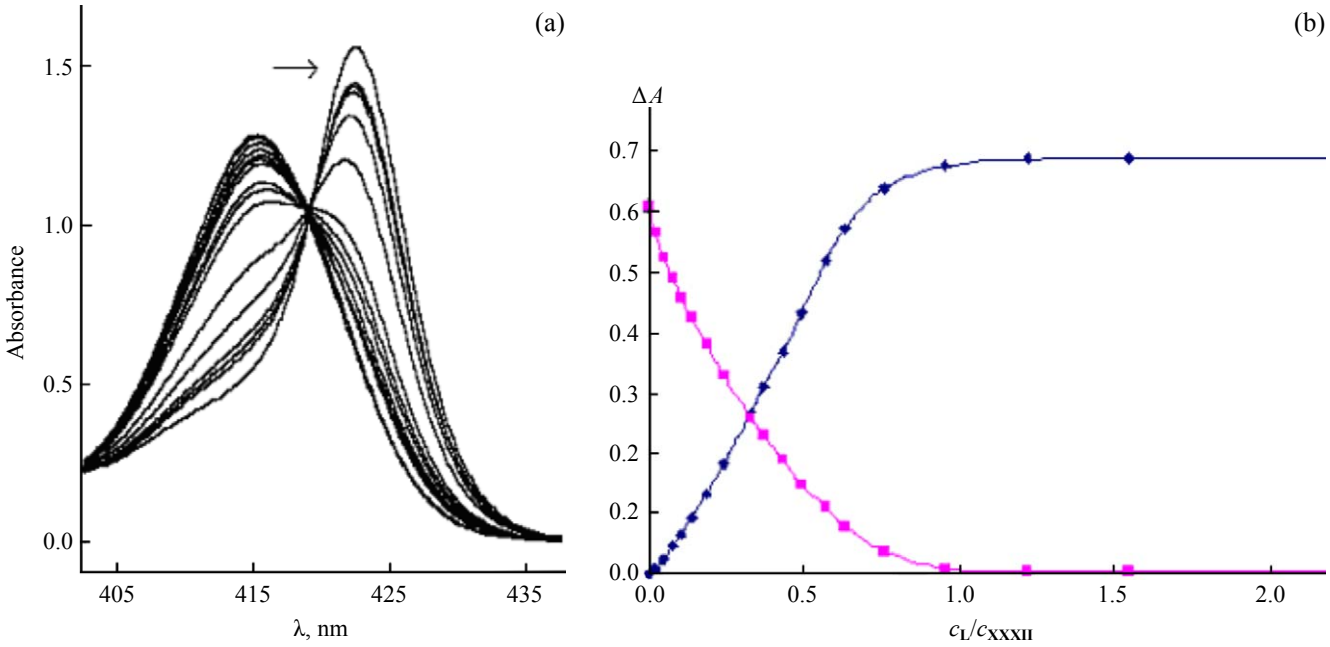
XXXII–L

indicating that the porphyrin fragments therein are not parallel but are arranged at some angle with respect to each other. Those β-protons in the porphyrin fragments, which appear closer to the calix[4]pyrrole moiety and are therefore closer to each other, are shielded to a greater extent by the porphyrin macrocycle, and the corresponding signals are located at δ 8.60 ppm (8H) (cf. δ 8.67 ppm for the other β-pyrrole protones). The NH protons in the calix[4]pyrrole fragments of **XXXI** and **XXXII** give a broadened singlet at δ 7.24 ppm, and all β-pyrrole protons in the calix[4]-pyrrole fragment resonated as one clearly defined doublet at δ ~5.72 ppm.

The Soret band in the electronic absorption spectrum of bis(porphyrin)–calix[4]pyrrole **XXXI** was displaced to the blue region (by up to 5 nm) and was characterized by reduced intensity and appreciable broadening as compared to porphyrins **XXVI** and **XXX**. These findings also indicated a fairly strong interaction between the π-electron systems of the porphyrin fragments in molecule **XXXI**.

In continuation of our studies in the field of supramolecular chemistry of macrocyclic compounds [21–23], we examined the complexing ability of conjugate **XXXII** toward 1,4-diazabicyclo[2.2.2]octane (L) in toluene by spectrophotometric titration and ^{1}H NMR (Scheme 9). We previously found [24] that compound **XXIII** with ligand L forms 1:2 complex **XXIII**–2L in which each porphyrin fragment coordinates one ligand molecule. Presumably, the distance between the porphyrin macrocycles in receptor molecule **XXIII** is too long to form a 1:1 complex where ligand L would be coordinated by both porphyrin fragments.

The formation of the 1:2 complex is confirmed by the presence in its ^{1}H NMR spectrum of signals belonging to nonequivalent protons of ligand L. Some protons that appear closer to the porphyrin macrocycle are shielded to a greater extent, and they give an upfield signal at δ –2.57 ppm. The other protons are more distant from the porphyrin macrocycle, and they do not suffer shielding effect of the latter, so that they resonate in a weaker field, at δ 0.97 ppm. The stability constant corresponding to coordination of one ligand molecule to one porphyrin fragment of the receptor is comparable with the stability constant of the complex formed by structurally similar monomeric metal porphyrin with the same diamine (160000 L/mol) [24].



(a) Variation of the electronic absorption spectra (Soret band region) of compound **XXXII** during complexation with 1,4-diazabicyclo[2.2.2]octane (L) in toluene and (b) spectrophotometric titration curves at descending and ascending wavelengths at 25°C.

Study of the complexation of **XXXII** with diamine L revealed formation of 1:1 complex **XXXII**–L. Only one chemical equilibrium was detected over a wide range of ligand concentrations (0 to 10×10^{-4} M), which established at a reactant molar ratio of 1:1 (see figure). Presumably, the lack of ethynyl fragment in the spacer connecting the porphyrin and calix[4]pyrrole fragments ensures closer arrangement of the porphyrin macrocycles in molecule **XXXII** as compared to **XXIII** and hence more favorable steric conditions for bidentate coordination of the ligand. This coordination scheme is confirmed by the observation of one isosbestic point family in the electronic spectra of the reaction system and of one jump on the corresponding spectrophotometric titration curve (see figure), by high stability constant of complex **XXXII**–L (K_s = 750000 L/mol), and by the presence of one upfield signal from the equivalent CH_2CH_2 protons of the ligand (δ –3.60 ppm).

EXPERIMENTAL

Commercial pyrrole, benzaldehyde, 4-acetylbenzaldehyde, 1,4-diazabicyclo[2.2.2]octane, and organic solvents (Sigma) were used without additional purification. The products were isolated by column chromatography on neutral aluminum oxide using methylene chloride–hexane or methylene chloride–benzene mixtures. The progress of reactions was monitored by TLC on Silufol UV-254 plates. The mass spectra (electron impact, 70 eV) were obtained on an MKh-1310 instrument (ion source temperature 150–200°C). The ^{1}H NMR spectra were recorded on a Bruker VC-500 spectrometer at 500.7 MHz using benzene-d_6 as solvent and tetramethylsilane as internal reference. The electronic absorption spectra were measured from solutions in toluene on a Varian Cary 100 spectrophotometer.

1-[4-(10,15,20-Triphenylporphyrin-5-yl)phenyl]-ethanone (XXVI). A mixture of 35 mL (0.50 mmol) of pyrrole, 38.1 mL (0.37 mmol) of benzaldehyde, 17.76 mg (0.12 mmol) of 4-acetylbenzaldehyde, and 1.5 g of chloroacetic acid in 350 mL of xylene was heated for 30 min under reflux in an argon atmosphere. The mixture was cooled, purged with air, and heated for 1 h under reflux. The resulting solution was cooled, washed with water, and evaporated under reduced pressure, and the residue was subjected to chromatography on aluminum oxide using methylene chloride–benzene (1:1) as eluent to isolate 1,1′-[10,20-diphenylporphyrin-5,15-diylbis(benzene-4,1-diyl)]diethanone, 1,1′,1″,1‴-[porphyrin-5,10,15,20-tetrayltetrakis(benzene-4,1-diyl)]tetraethanone, 5,10,15,20-tetraphenylporphyrin, and compound **XXVI**. Yield of **XXVI** 7.14 mg (9%), R_f 0.41 (Al_2O_3, CH_2Cl_2–benzene, 1:1). Electronic absorption spectrum (toluene), λ_{max}, nm (logε): 648 (3.65), 592 (3.99), 550 (4.29), 516 (4.69), 419 (5.03). ^{1}H NMR spectrum, δ, ppm: 8.70 br.s (8H,

β-H), 7.33 d (8H, *o*-H), 7.76 m (11H, *m*-H, *p*-H), 1.40 s (3H, CH_3), 2.81 s (2H, NH). Mass spectrum: *m*/*z* 657.5 $[M]^+$.

5-[4-(5-Methyldipyrrometan-5-yl)phenyl]-10,15,20-triphenylporphyrin (XXX). A solution of 5.26 mL of (0.075 mmol) of pyrrole in 50 mL of ethanol was added dropwise under stirring to a solution of 9.66 mg (0.015 mmol) of compound **XXVI** in 100 mL of ethanol–methylene chloride (5:1 by volume). The mixture was heated to the boiling point, 2 mL of aqueous HCl was added, and the mixture was heated for 30 min under reflux, cooled, and diluted with 150 mL of water. The organic phase was separated and washed with water, and the solvent was removed under reduced pressure. The residue was subjected to chromatography on aluminum oxide using methylene chloride–hexane (1:1) as eluent. The eluate was evaporated under reduced pressure, and the oily residue was brought into the next step without additional purification. Electronic absorption spectrum (toluene), λ_{max}, nm (logε): 647 (3.62), 591 (3.96), 549 (4.27), 515 (4.53), 418 (5.01). ^{1}H NMR spectrum, δ, ppm: 8.72 br.s (8H, β-H), 7.36 d (8H, *o*-H), 7.79 m (11H, *m*-H, *p*-H), 7.21 br.s (2H, NH, pyrrole), 6.18 s (2H, α-H, pyrrole), 5.70 d (4H, β-H, pyrrole), 1.44 s (3H, CH_3), 2.83 s (2H, NH, porphyrin).

2,2,4,6,6,8-Hexamethyl-4,8-bis[4-(10,15,20-triphenylporphyrin-5-yl)phenyl]-1,3,5,7(2,5)-tetrapyrrolacyclooctaphane (XXXI). Trifluoroacetic acid, 1 mL, was added under stirring to a mixture of 10 mg of compound **XXX** and 50 mL of acetone, and the mixture was stirred for 30 min at room temperature. The mixture was then treated in succession with 20 mL of 10% aqueous K_2CO_3 and 50 mL of methylene chloride, and the organic phase was separated, washed with water, dried over Na_2SO_4, and subjected to chromatography on aluminum oxide using methylene chloride–hexane (1:2) as eluent. Yield 5.7 mg (48%), R_f 0.53 (Al_2O_3, CH_2Cl_2–hexane, 1:2). Electronic absorption spectrum (toluene), λ_{max}, nm (logε): 644 (3.31), 590 (3.87), 548 (4.08), 513 (4.33), 414 (4.81). ^{1}H NMR spectrum, δ, ppm: 8.67 br.s and 8.60 br.s (8H each, β-H), 7.31 d (16H, *o*-H), 7.74 m (22H, *m*-H, *p*-H), 7.24 br.s (4H, NH, calixpyrrole), 5.72 d (8H, β-H, calixpyrrole), 0.42 s (12H, CH_3), –0.39 s (6H, CH_3), 2.89 br.s (4H, NH, porphyrin). Mass spectrum: *m*/*z* 1625.3 $[M]^+$.

5,5′-[2,4,4,6,8,8-Hexamethyl-1,3,5,7(2,5)-tetrapyrrolacyclooctaphane-2,6-diylbis(benzene-4,1-diyl)]bis[(10,15,20-triphenylporphyrinato)zinc] (XXXII). Compound **XXXI**, 5 mg, was dissolved in 70 mL of dimethylformamide, excess (10 equiv) of zinc acetate was added, and the mixture was heated for 30 min under reflux. The mixture was cooled and diluted with an equal volume of water, and the precipitate was filtered off, dried, and subjected to chromatography on aluminum oxide using methylene chloride–hexane (1:2) as eluent. The eluate was evaporated under reduced pressure, and the residue was recrystallized from methylene chloride–methanol (1:1). Yield 4.5 mg (90%), R_f 0.45 (Al_2O_3, CH_2Cl_2–hexane, 1:2). Electronic absorption spectrum (toluene), λ_{max}, nm (logε): 588 (3.87), 548 (4.08), 416 (4.81). ^{1}H NMR spectrum, δ, ppm: 8.66 br.s (8H, β-H), 8.59 br.s (8H, β-H), 7.30 d (16H, *o*-H), 7.72 m (22H, *m*-H, *p*-H), 7.23 br.s (4H, NH, calixpyrrole), 5.70 d (8H, β-H, calixpyrrole), 0.41 s (12H, CH_3), –0.37 s (6H, CH_3). Mass spectrum: *m*/*z* 1756.9 $[M]^+$.

The stability constants of the bis[porphyrinato(zinc)] complexes with 1,4-diazabicyclo[2.2.2]octane (L) were determined by spectrophotometric titration using the following equation [25]:

$$K_s = \frac{[\mathbf{A}\cdot\mathbf{B}]}{[\mathbf{A}]\,[\mathbf{B}]} = \frac{1}{[\mathbf{B}]}\left(\frac{\Delta A_{i,\lambda 1}}{\Delta A_{0,\lambda 1}}\,\frac{\Delta A_{0,\lambda 2}}{\Delta A_{i,\lambda 2}}\right)\text{(L/mol)}.$$

Here, λ_1 is a descending wavelength, λ_2 is an ascending wavelength, [**A**] is the concentration of bis[(porphyrinato)zinc]–calix[4]pyrrole, [**B**] is the ligand concentration, ΔA_0 is the maximum variation of the optical density at a given wavelength, and ΔA_i is the variation of the optical density at a given wavelength at a given concentration.

This study was performed under financial support by the Russian Foundation for Basic Research (project nos. 12-03-00775, 14-03-00011, 14-03-00009), by the Chemistry and Materials Science Department of the Russian Academy of Sciences (program no. 6, "Chemistry and Physical Chemistry of Supramolecular Systems and Atom Clusters"), and by the Presidium of the Russian Academy of Sciences (program no. 24, "Nanodrugs and Their Targeted Delivery") with the use of the facilities provided by the center for joint use of scientific equipment "The Upper Volga Region Center of Physicochemical Research."

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